Letter to the Editor

Prevalence of cardiovascular events in diabetic patients taking sulphonylureas: need for assessment

Madam, ATP-sensitive K+ (KATP) channels have been shown to play an important role in different cells during physiologic as well as pathophysiologic processes; thus making them a valuable therapeutic target. These channels are widely distributed in various cell types including pancreatic cells, vascular smooth muscle cells, endothelial cells, cardiomyocytes, neurons and others. Sulphonylurea drugs, widely used in the treatment of type 2 diabetes mellitus induce the closure of KATP channels thus inhibiting the K+ conductance across the plasma membrane of cells of pancreas. The resulting membrane depolarization enhances insulin secretion. Here, we are postulating a potential problem associated with the use of KATP channel inhibitors especially the non-selective ones like older generation sulphonylureas. These drugs can produce undesirable effects by interacting with KATP channels expressed on plasma membrane of cells other than pancreatic cells. The KATP channels not only play an important role in regulation of coronary blood flow but also protect cardiac cells from ischaemia/reperfusion injury. Evidence that KATP channels are active under resting conditions and contribute to maintenance of basal coronary vascular tone comes from studies of blood flow in canine hearts in vivo[1], and in isolated perfused rabbit hearts.[2] By virtue of their regulation by cellular metabolism, KATP channels are also likely to play an important role in the alterations in cellular function that occur during pathophysiological stresses, such as hypoxia, ischaemia and septic shock.[3] We have also shown that acidosis induces the relaxation of human internal mammary artery via opening of KATP channel, which is completely blocked by pretreatment with glibenclamide.[4]

Sulphonylureas are used in the treatment of type II diabetes mellitus. Although achieving optimum blood glucose levels with the use of sulfonylureas is a desirable therapeutic goal, extra-pancreatic action of these drugs need to be carefully studied. It has been observed that diabetes is already associated with reduced function of vascular KATP channels.[5] In the face of already impaired KATP channel function, the assumption that diabetic patients taking KATP channel inhibitors, sulphonylureas especially the ones with less selectivity are at risk of developing or worsening of coronary artery disease needs close monitoring. However, there are few studies, which have shown positive correlationship between the intake of sulphonylureas and the adverse cardiovascular profile in preliminary studies.[6] We conclude that since KATP channels have a diverse distribution in the body, tissue selectivity of the modifiers of KATP channels is of utmost importance in treatment. Furthermore, the studies should be conducted to quantify the development of potential problems associated with the blockade of extra-pancreatic KATP channels, specially the cardiovascular events in diabetic patients taking sulphonylureas.

Dileep Kumar Rohra[1], Archana Raysee Maheshwary[2], Sonia Shamlal Gauba[3]
Department of Biological and Biomedical Sciences, Aga. Khan University[1], Karachi, Jinnah Medical and Dental College[2], Karachi, Chandka Medical College[3], Larkana.

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